REGIONAL VARIATION IN MYOCARDIAL ACCUMULATION OF ^{18}F-FLUORODEOXYGLUCOSE IN FASTED NORMAL SUBJECTS.

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Positron emission tomography utilizing ^{18}F-fluorodeoxyglucose (FDG) has been used for identifying jeopardized but viable myocardium. It has been assumed that the regional distribution of FDG accumulation (FDG-A) in the normal heart is relatively homogeneous and independent of levels of circulating substrates. However, in initial studies of fasted normal humans we observed large regional disparities in myocardial FDG-A. Accordingly, we assessed regional myocardial glycolytic flux with FDG and referenced it to regional perfusion (MBF) with $H_2{}^{15}O$ and oxidative metabolism [^{11}C-acetate (AC)] in 9 normal subjects, 4 studied after a 5-hour fast and 5 studied both fasted and fed. Septum-to-lateral wall ratios (SLR; mean ± SD) were determined for FDG-A, AC accumulation (AC-A) and clearance (AC-C), and MBF. Under fasting conditions regional disparities in FDG-A were noted (SLR of .72 ± .11), that diminished significantly with feeding (SLR of .90 ± .08, p < .05). With fasting, MBF, AC-A and AC-C were homogeneous (SLR of .95 ± .3, .98 ± .07, .9 ± .09, respectively; p < .05 compared to fasting FDG-A SLR), and did not change significantly under fed conditions (SLR of 1.1 ± .3, 1.1 ± .06, 1.0 ± .16, respectively). Thus, under fasting conditions there are significant regional variations in myocardial glycolytic flux, which are independent of oxidative metabolism or perfusion and which cannot be attributed to partial volume effects (since AC accumulation was spatially homogeneous). These regional disparities in FDG-A seen under fasting conditions must be considered in analysis of data so acquired.

QUANTITATIVE PET MEASUREMENT OF DIPYRIDAMOLE VASODILATORY CAPACITY IN HUMANS.

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We previously validated a method to measure myocardial blood flow (MBF) employing dynamic multislice positron emission tomography (PET) and ^{15}O-labelled water in a dog model against simultaneous measurements of MBF with microspheres (r = 0.97). To determine the feasibility of this method during myocardial hyperemia in humans, we studied 7 healthy volunteers (N) (mean age 30 ± 5 years) at rest and after I.V. administration of 0.6 mg/Kg x 4mins of dipyridamole (D). Over 50 regions of interest (ROI) were drawn on an average of 8 cross-sectional images of the heart to generate time/activity curves of the myocardium and left ventricular chamber (arterial imput function) and MBF was obtained by fitting the data to a 2 compartment model. MBF measurements were grouped in 4 myocardial regions (anterior, lateral, inferior-posterior, septal). Regional MBF at rest ranged from 0.61 to 1.25 ml/g/min (mean 0.88 ± 0.13 ml/g/min) and the rate-pressure product (RPP) from 5760 to 10440 bpm x mmHg (mean 7758 ± 1462 bpm x mmHg). After D MBF increased significantly in all regions ($p < 0.0001$) ranging from 2.03 to 4.91 ml/g/min (mean 3.58 ± 0.84 ml/g/min); the rate-pressure product increased significantly ($p < 0.05$) ranging from 8500 to 12650 bpm x mmHg (mean 10104 ± 1462 bpm x mmHg). Mean coronary flow reserve (MBF after D/MBF at rest) ranged from 2.78 to 5.21 (mean 4.12 ± 0.9); however no significant differences were seen in RPP at rest or after D between subjects with high and reduced coronary flow reserve (p = NS). Thus assessment of MBF with $H_2{}^{15}O$ and PET permits detection of the differences in blood flow, induced by vasodilator stress. This non-invasive procedure should therefore prove useful for the assessment of clinical interventions designed to augment regional perfusion.

ATTENUATED RESPONSE OF GLUCOSE METABOLISM IN REPERFUSED CANINE MYOCARDIUM TO CHANGES IN SUBSTRATE LEVELS.

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Fluoro-2-deoxyglucose (FDG) is used with PET to measure regional glucose utilization and to study altered glucose metabolism in ischemic injury. However, the effects of substrate availability on these measurements have not been systematically examined. In 10 closed chest dogs, the proximal LAD was occluded with an intracoronary balloon for 20 min. On day 2, 5 dogs were maintained at steady state euglycemic (EUG) levels (125±10 mg/dl) and 5 dogs at hyperglycemic (HYPG) levels (184±9.6 mg/dl). FDG was injected and the arterial input function obtained. Microsphere blood flow was measured during occlusion and prior to FDG. Wall motion by echocardiography was abnormal in all 10 dogs 30 min after reperfusion (stunning) and in 8 of 10 dogs prior to FDG. TTC staining of reperfused myocardium (RM) revealed subendocardial necrosis in 1 dog and speckled anterior papillary muscle necrosis in 3 dogs. Tissue FDG activity in control and RM was converted to metabolic rate (MR, mg/min/100gm). Occlusion blood flows were similar in HYPG and EUG dogs in control (1.7±0.6 vs 1.4±0.5 ml/min/gm; NS) and RM (0.5±0.48 vs 0.38±0.25 ml/min/gm; NS). MR in HYPG dogs was 4-6 fold higher than in EUG dogs in control (50.5±23.1 vs 8.9±6.4; p<0.005) and RM (37.6±19.4 vs 11.4±7.2; p<0.025). Relative to control tissue, MR in RM was 58±58% higher in EUG dogs but 24±17% lower in HYPG dogs (p<0.01). Thus, glucose utilization in reperfused myocardium is elevated during euglycemia, but increases disproportionately less than in control myocardium in HYPG. The results are consistent with altered glucose metabolism in RM which depends less than normal myocardium on substrate availability. They also indicate that metabolic evaluation of RM requires knowledge of substrate levels.

MEASUREMENT OF MYOCARDIAL PERFUSION WITH POSITRON EMISSION TOMOGRAPHY AND GENERATOR-PRODUCED COPPER-62-PTSM

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A number of cardiac PET centers are using rubidium-82 (^{82}Rb) for estimates of myocardial blood flow (MBF). Since myocardial metabolism significantly influences and therefore limits the use of ^{82}Rb as a flow tracer, we have been evaluating copper-(II)bis(N^4-methyl thiosemicarbazone)(Cu-PTSM) for quantitative estimates of MBF. In intact dogs with induced left anterior descending coronary stenoses, we evaluated noninvasively with PET the myocardial extraction of generator-produced ^{62}Cu-PTSM ($t_{1/2}$ = 9.8 min) at rest and after hyperemia induced with intravenous dipyridamole. Extraction (E) of ^{62}Cu-PTSM administered i.v. varied inversely with flow (assessed independently with radiolabeled microspheres) ($E = 0.66e^{-0.347MBF}$) (n = 15 measurements, r = 0.93). Once extracted, retention of tracer by the heart was persistent. Blood pool clearance was rapid (< 10% of peak by 3 min) yielding excellent quality images and clear delineation of regions subtended by stenoses. In an initial study in a normal human subject, myocardial extraction of ^{62}Cu-PTSM averaged 20 ± 3% (n = 10 regions). Blood pool clearance was rapid and myocardial retention of extracted tracer homogeneous and prolonged, yielding excellent myocardial images which were concordant with the distribution of $H_2{}^{15}O$. The results of this study suggest that ^{62}Cu-PTSM, a generator-produced positron emitting radioisotope, should permit quantitative estimates of regional MBF with PET in humans.